SUPPLEMENT ARTICLE

Hospitalized Patients with 2009 Pandemic Influenza A (H1N1) Virus Infection in the United States—September–October 2009

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Given the potential worsening clinical severity of 2009 pandemic influenza A (H1N1) virus (pH1N1) infection from spring to fall 2009, we conducted a clinical case series among patients hospitalized with pH1N1 infection from September through October 2009. A case patient was defined as a hospitalized person who had test results positive for pH1N1 virus by real-time reverse-transcription polymerase chain reaction. Among 255 hospitalized patients, 34% were admitted to an intensive care unit and 8% died. Thirty-four percent of patients were children <18 years of age, 8% were adults ≥65 years of age, and 67% had an underlying medical condition. Chest radiographs obtained at hospital admission that had findings that were consistent with pneumonia were noted in 103 (46%) of 255 patients. Among 255 hospitalized patients, 208 (82%) received neuraminidase inhibitors, but only 47% had treatment started ≤2 days after illness onset. Overall, characteristics of hospitalized patients with pH1N1 infection in fall 2009 were similar to characteristics of patients hospitalized with pH1N1 infection in spring 2009, which suggests that clinical severity did not change substantially over this period.

On 15 April and 17 April 2009, the Centers for Disease Control and Prevention (CDC) confirmed the first 2 cases of human infection with 2009 pandemic influenza A (H1N1) virus (pH1N1) in the United States [1]. pH1N1 contains a unique combination of gene segments not previously recognized among humans or animals [2, 3] and has spread throughout the world since spring 2009 [4]. In the United States, a small spring wave was followed by widespread pH1N1 activity in the fall [5].

The clinical spectrum of illness and risk factors for severity among persons hospitalized with pH1N1 infection during spring 2009 has been described [6–8]. As previously observed with seasonal influenza, most patients hospitalized with pH1N1 infection had underlying medical conditions, such as diabetes or cardiovascular, neurologic, and pulmonary disease, including asthma [9–11]. In contrast to the age distribution of seasonal influenza hospitalizations, persons ≥65 years of age were less likely than other age groups to be hospitalized with pH1N1 infection [6–8]. From 3

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

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Clinical Infectious Diseases 2011;52(S1):S50–S59
Published by Oxford University Press on behalf of the Infectious Diseases Society of America 2011.
1058-4838/2011/52S1-0001$37.00
DOI: 10.1093/cid/ciq021

pH1N1 influenza hospitalization case series conducted in spring 2009, frequency of intensive care unit (ICU) admission and death among those hospitalized ranged from 24%–31% and from 4%–11%, respectively [6–8].

Measures of illness severity, such as the proportion of hospitalized patients admitted to the ICU and the overall hospitalized patient fatality proportion, are essential for decision making and to help inform planning for health care surge and response during the progression of a pandemic. In past pandemics, severity of illness changed during multiple waves of infection [12]. Most notable is the 1918 influenza pandemic, when, after a mild spring wave of infection, more-severe disease was documented in the fall of 1918 [13, 14]. It is unclear whether the increased severity of illness in 1918 was due to viral evolution, an increasing number of bacterial co-infections, or other factors [13]. Given the potential for worsening clinical severity during the pH1N1 pandemic, continued surveillance for signs of increasing severity was critical. This report summarizes the clinical characteristics of patients hospitalized with pH1N1 infection in the United States during the second, or fall, pandemic wave.

METHODS

A case patient was defined as a person hospitalized with laboratory-confirmed pH1N1 infection as determined by real-time reverse-transcription polymerase chain reaction from 1 September through 31 October 2009. Laboratory testing was performed at state health departments using CDC-based primers [15]. From 1 September to 31 October 2009, a total of 17,828 pH1N1-associated hospitalizations in the United States were reported to the CDC [5]. From these 17,828 hospitalizations, we sampled 300 hospitalized case patients from all 50 states and the District of Columbia with the probability of selection proportional to the number of hospitalized pH1N1 case patients reported to the CDC by each reporting jurisdiction. Using this sampling strategy, 45 states were selected to participate, and each state was asked to provide information for a specified number of hospitalized case patients. Each participating state randomly selected the requested number of case patients from their confirmed pH1N1-associated hospitalizations. State and local public health officials were asked to conduct a medical chart review using a standardized data collection instrument for each hospitalized case patient to assess severity; participation was voluntary. Medical chart reviews and abstractions were performed by infection control practitioners, physicians, nurses, and epidemiologists at local and state public health departments. Data collection included demographic characteristics, influenza vaccination history, underlying medical conditions that conferred a higher risk of influenza complications [16], clinical signs and symptoms, select laboratory tests, radiographic findings, and treatment course. All diagnostic testing was performed as part of routine clinical management. The protocol and standardized clinical form were approved by the CDC's institutional review board. In addition, this case series was part of the emergency public health practice response to the pandemic and was reviewed by a human subjects coordinator at the CDC and deemed not to be research in accordance with the federal human subjects protection regulations at 45 Code of Federal Regulations 46.101c and 46.102d and the CDC's Guidelines for Defining Public Health Research and Public Health Non-Research.

Key measures of severity were proportion of hospitalized patients admitted to the ICU and the overall hospitalized case fatality proportion. In addition, we conducted bivariate analysis, comparing non-ICU patients who survived with patients who died or were admitted to the ICU; the χ^2 test was used to compare categorical variables, and the Wilcoxon rank-sum test was used to compare continuous variables ($\alpha = .05$). We used multivariable logistic regression models to further investigate associations with severity. All analyses were conducted in SAS, version 9.2 (SAS Institute).

RESULTS

Clinical Characteristics

This report describes 255 completed chart abstractions of hospitalized case patients with confirmed pH1N1 infection reported to the CDC from the 40 (275 case patients sampled) of 45 states that agreed to participate in this case series. Dates of illness onset ranged from 25 August 2009 to 31 October 2009. The median age of patients was 28 years (Table 1). The majority of patients were non-Hispanic white (48%) or black (22%).

Symptoms and reported signs at presentation included fever and cough (Table 2). Diarrhea or vomiting was reported in 41% of patients, including 51% of children aged <18 years and 36% of adults aged ⩾18 years. The median time from illness onset to hospital admission was 2 days (range, 0–27 days). One-hundred-seventy patients (67%) had an underlying medical condition conferring a higher risk of influenza complications (Table 2), including 48% of children aged <18 years and 76% of adults aged ⩾18 years; 32% had ⩾2 conditions. Among those aged ⩾65 years, 80% had an underlying condition. Asthma was the most common underlying condition seen in children (24%) and adults (25%). Neurologic disorders, including neurocognitive (developmental delay and dementia), neuromuscular, or seizure disorders, were prevalent in both groups (14%). Twenty-nine patients (11%) were pregnant; 8 (28%) had another underlying condition, including asthma (5 patients) and diabetes (2).

Height and weight or obesity status were available for 185 (95%) of 195 non-pregnant persons aged ⩾2 years. Among 132 adults, 77 (58%) had a body mass index (BMI, calculated as the

Table 1. Characteristics of Hospitalized Patients Infected with 2009 Pandemic Influenza A (H1N1) Virus – United States, September–October 2009

Variable	Patients (n = 255)
Female sex	145 (57)
Age, median years (range)	28 (1 month to 87 years)
Age group	
0–23 Months	31 (12)
2–4 Years	11 (4)
5–9 Years	22 (9)
10–17 Years	22 (9)
18–49 Years	114 (45)
50–64 Years	35 (14)
⩾ 65 Years	20 (8)
Race and ethnicity	
Hispanic	43 (17)
Non-Hispanic White	122 (48)
Black	55 (22)
Native Hawaiian, Asian, or Pacific Islander	6 (2)
Native American	0 (0)
Multiracial, not further defined	2 (1)
Unspecified	27 (11)

NOTE. Data are no. (%) of patients, unless otherwise indicated.

weight in kilograms divided by the square of height in meters) ⩾30, with 48 (36%) being obese (BMI 30.0–39.9) and 29 (22%) being morbidly obese (BMI ⩾40) (Table 2); 33 (69%) of 48 of the obese and 22 (76%) of 29 of the morbidly obese had an underlying condition. Among 53 children, 7 (13%) were obese (BMI percentile 95–100), 4 (57%) of whom had an underlying condition.

Radiologic Findings at Hospital Admission

A total of 103 (46%) of 225 patients for whom hospital admission chest radiograph reports were performed had findings that were consistent with pneumonia; the median age was 28 years (range, 1 month to 71 years), and 62% of patients with pneumonia had an underlying medical condition. Radiographic findings included bilateral interstitial infiltrates (31%), a lobar infiltrate limited to 1 lobe (30%), and bilateral lobar infiltrates (17%).

Treatment

Among 255 hospitalized patients, 208 (82%) received treatment with neuraminidase inhibitors (Table 2). One-hundred-ninety-two patients received oseltamivir alone, and 3 received zanamivir alone; 3 patients received therapy with amantadine plus oseltamivir, 1 received therapy with rimantadine plus oseltamivir, 2 received therapy with peramivir plus oseltamivir, and 7 received therapy with zanamivir and oseltamivir. The median time from illness onset to antiviral initiation was 3 days (range, 0–27 days); 47% of patients received antivirals within 2 days of illness onset. For 206 patients for whom antiviral initiation date was available, receipt of antivirals in relation to hospital admission was as follows: before admission, 7 patients (3%); at admission, 128 (62%); within 2 days of admission, 51 (25%); and >2 days after admission, 20 (10%).

Among 255 hospitalized patients, 186 (73%) received antibiotics. For 182 patients for whom antibiotic initiation date was available, receipt of antibiotics in relation to hospital admission was the following: before admission, 14 patients (8%); at admission, 124 (68%); within 2 days of admission, 38 (21%); and >2 days after admission, 6 (3%). Patients received a median of 2 antibiotics (range, 1–5); 67% of patients received >1 antibiotic. Commonly used antibiotics included ceftriaxone (44%), azithromycin (38%), vancomycin (30%), and levofloxacin (29%). Of patients with radiograph findings consistent with pneumonia, 83% were treated with antivirals and 83% were treated with antibiotics.

Among 255 hospitalized patients, 93 (36%) received steroids: oral steroids in 24 patients, intravenous steroids in 27 patients, oral and intravenous steroids in 28 patients, and route unspecified in 14 patients. Seventy-eight percent of patients who received steroids had an underlying condition; asthma or chronic obstructive pulmonary disease (COPD) (60%), diabetes (24%), and cardiovascular disease (17%) were the most common underlying conditions.

Diagnostic Findings

At hospital admission, 44 patients (19%) were leukopenic, 104 (46%) were anemic, and 55 (24%) were thrombocytopenic (Table 3). Of 156 patients with information on blood cultures obtained at hospital admission, 6 patients (4%) had positive blood culture results at hospital admission: 2 patients (a 2-year-old male and an 11-year-old female) with methicillin-resistant *Staphylococcus aureus* (MRSA) infection, 3 patients (a 13-year-old female, a 34-year-old female, and an 83-year-old female) with methicillin-sensitive *S. aureus* (MSSA) infection, and 1 patient (a 58-year-old male) with infection due to *S. aureus* with unknown methicillin sensitivity; all patients survived to hospital discharge. Of the 73 patients with cultures obtained from the respiratory tract at hospital admission, 3 patients (4%) had microbiological evidence of infection: a 5-year-old girl who had multiorgan system failure and died within 24 h after admission had *Streptococcus pneumoniae* isolated from a tracheal aspirate, an 11-year-old boy who had bilateral pneumonia requiring mechanical ventilation and survived to discharge had *Moraxella catarrhalis* isolated from a lower respiratory tract specimen; and a 55-year-old man who had received a renal transplant and was receiving immunosuppressive agents who presented with bilateral lobar infiltrates visible on a chest radiograph obtained at hospital admission and survived to hospital discharge had *S. pneumoniae* isolated from a sputum culture.

ICU Admissions

Eighty-six patients (34%) were admitted to the ICU, and 18 (21%) died. The median age was 31.5 years (range, 10 months to 70 years). The majority of ICU patients had an underlying high-risk condition (54 [63%] of 86); asthma or COPD (34%), chronic cardiovascular disease (17%), and diabetes (16%) were most common. Five (6%) of 86 ICU patients were pregnant; 1 was in the second trimester, 3 were in the third trimester, and 1 was in an unknown trimester. Of those admitted to the ICU, 46 patients (53%) required mechanical ventilation, 25 (29%) had acute respiratory distress syndrome (ARDS), and 14 (16%) had a clinical diagnosis of sepsis. Of those admitted to the ICU, 73 patients (85%) received antiviral treatment and 79 (92%) received antibiotics. The median time from illness onset to antiviral initiation was 4 days (range, 0–16 days), with only 33% of patients receiving antivirals within 2 days of illness onset.

Outcomes

Among 255 hospitalized patients in this case series, 21 (8%) died, 18 of whom were admitted to the ICU and 15 of whom

Table 2. Comparison of Clinical Characteristics of Patients Hospitalized with 2009 Pandemic Influenza A (H1N1) Virus Infection, United States, September–October 2009, by Age

Variable	All hospitalized patients (n = 255)	Children <18 years of age (n = 86)	Adults ⩾18 years of age (n = 169)
Age, median years (range)	28 (1 month to 87 years)	5 (1 month to 17 years)	42 (18 to 87 years)
Time from illness onset to hospital admission, median days (range)[a]	2 (0–27) (n = 254)	2 (0–27) (n = 85)	3 (0–21)
Length of hospital stay, median days (range)[a]	3 (0–73) (n = 252)	2 (0–57) (n = 85)	3 (0–73) (n = 167)
Time from illness onset to discharge or death, median days (range)[a]	6 (0–82) (n = 251)	4.5 (1–57) (n = 84)	7 (0–82) (n = 167)
Clinical symptoms at hospital admission			
Fever	222 (87)	82 (95)	140 (83)
Cough	219 (86)	66 (77)	153 (91)
Shortness of breath	139 (55)	39 (45)	100 (59)
Wheezing	75 (29)	23 (27)	52 (31)
Fatigue/weakness	92 (36)	24 (28)	68 (40)
Chills	76 (30)	13 (15)	63 (37)
Myalgias	85 (33)	10 (12)	75 (44)
Headache	62 (24)	14 (16)	48 (28)
Altered mental status	25 (10)	10 (12)	15 (9)
Conjunctivitis	5 (2)	1 (1)	4 (2)
Sore throat	67 (26)	18 (21)	49 (29)
Rhinorrhea	95 (37)	42 (49)	53 (31)
Vomiting	82 (32)	38 (44)	44 (26)
Diarrhea	48 (19)	12 (14)	36 (21)
Underlying medical conditions[b]			
Any one condition	170 (67)	41 (48)	129 (76)
Asthma	63 (25)	21 (24)	42 (25)
Chronic obstructive pulmonary disease	27 (11)	0 (0)	27 (16)
Other lung disease	11 (4)	4 (5)	7 (4)
Diabetes	33 (13)	0 (0)	33 (20)
Immunocompromise	21 (8)	2 (2)	19 (11)
Chronic cardiovascular disease	35 (14)	4 (5)	31 (18)
Chronic renal disease	17 (7)	5 (6)	12 (7)
Neurocognitive disorder	17 (7)	7 (8)	10 (6)
Neuromuscular disorder	19 (7)	8 (9)	11 (7)
Seizure disorder	14 (5)	6 (7)	8 (5)
Pregnancy	29 (11)	1 (1)	28 (17)
Current smoker[b]	46/244 (19)	0/85 (0)	46/159 (29)
Obese[c]	55/185 (30)	7/53 (13)	48/132 (36)
Morbidly obese[c]	29/185 (16)	NA	29/132(22)
Influenza vaccination for seasonal influenza	30/174 (17)	10/60 (17)	20/114 (18)
Influenza vaccination for 2009 H1N1	5/152 (3)	2/57 (4)	3/95 (3)

Hospitalization results			
Chest radiograph findings consistent with pneumonia at hospital admission	103/225 (46)	36/74 (48)	67/151 (44)
Acute respiratory distress syndrome	26/239 (11)	6/84 (7)	20/155 (13)
Diagnosis of sepsis at hospital admission	17/242 (7)	4/84 (5)	13/158 (8)
Admitted to the intensive care unit	86/252 (34)	21/85 (25)	65/167 (39)
Invasive mechanical ventilation	47/244 (19)	12/85 (14)	35/159 (22)
Treated with antivirals	208 (82)	66 (77)	142 (84)
Treated with antivirals within 2 days of illness onset	96/206 (47)	38/66 (58)	59/140 (42)
Treated with antibiotics	186 (73)	57 (66)	129 (76)
Treated with steroids	93 (36)	29 (34)	64 (38)
Death	21 (8)	4 (5)	17 (10)
Among those treated with antivirals, days from illness onset to initiation of antivirals, median days (range)	3 (0–27) (n = 206)	2 (0–27) (n = 66)	3 (1–21) (n = 140)

NOTE. Data are no. (%) of patients, unless otherwise indicated. Overall missing data for different categories varied. For symptoms, there were 2%–19% of patients with missing data; for underlying conditions, there were 2%–3% with missing data; for influenza vaccination status, there were 32% with missing data; for obesity, there were 5% with missing data; and for hospitalization results, there were 2%–13% with missing data.

[a] Day of hospital admission was considered hospital day 0.

[b] Patients who were pregnant, immunocompromised (either due to medications or immune disorders including human immunodeficiency syndrome), or have chronic pulmonary (including asthma or chronic obstructive pulmonary disease), cardiovascular (excludes hypertension), renal, hepatic, hematological, neurological, or metabolic disease (including diabetes) were considered at high-risk for influenza-related complications. Patients who were current smokers or obese were not included in groups considered at high-risk for influenza complications.

[c] Body mass index (BMI), calculated as weight in kilograms divided by the square of height in meters, was determined for a subset of patients for whom height and weight data were available to determine obesity (BMI 30–39.9 in adults ⩾18 years or BMI percentile 95–100 in children 2–18 years old) and morbid obesity (BMI ⩾40 in adults only); pregnant women were excluded from this calculation.

required mechanical ventilation. The median age of patients who died was 34 years (range, 1–70 years); the median time from illness onset to death was 10 days (range, 3–83 days). Sixty-two percent of the patients who died had an underlying condition; cardiovascular disease (33%), diabetes (24%), immunosuppression (19%), and asthma or COPD (19%) were most common. Of those who died, 76% received antivirals and 95% received antibiotics. The median time from illness onset to antiviral initiation was 5.5 days (range, 2–16 days), and only 14% received antivirals within 2 days of illness onset.

Patients who were admitted to an ICU or died were significantly more likely than patients who were not admitted to an

Table 3. Select Laboratory Abnormalities for Hospitalized Patients with 2009 Pandemic Influenza A (H1N1) Virus Infection, United States, September–October 2009

Laboratory abnormality	Proportion (%) of patients
Leukopenia (white blood cell count <5000 cells/mm^3)	44/231 (19)
Leukocytosis (white blood cell count >11,000 cells/mm^3)[a]	52/231 (23)
Anemia[b]	104/228 (46)
Thrombocytopenia (<150,000 cells/mm^3)	55/231 (24)
Thrombocytosis (>350,000 cells/mm^3)	17/231 (7)
Elevated alanine aminotransferase level[c] Alanine aminotransferase level ⩾2 times the upper level of normal	64/125 (51) 21/125 (17)
Elevated asparate aminotransferase[§] Asparate aminotransferase level ⩾2 times the upper level of normal	58/127 (46) 21/127 (17)
Total bilirubin >1.2 mg/dL	12/122 (10)
Hyponatremia (serum sodium level <135 mmol/L)	62/216 (29)

NOTE. Laboratory ranges were based on Custer et al [45].

[a] Excluded newborns up to 28 days of age.

[b] Anemia is based on hematocrit. For adults ⩾19 years of age, hematocrit <41% for male individuals and <36% for female individuals is considered to be anemia. For children, age-based anemia was defined as follows: 12–18 years of age, hematocrit <36% for male individuals and <37% for female individuals; 6–11 years of age, hematocrit <35%; 2–5 years of age, hematocrit <34%; 6 months through 2 years of age, hematocrit <33%; 2 months through 6 months of age, hematocrit <31%; 1 month through 2 months of age, hematocrit <28%; and <1 month of age, hematocrit <33%.

[c] Elevated alanine aminotransferase level was defined as >30 U/L for patients ⩾1year of age and >54 U/L for patients <1 year of age. Elevated asparate aminotransferase level was defined as >35 U/L for patients ⩾1year of age and >65 for patients <1 year of age.

ICU to have shortness of breath, diarrhea, altered mental status, radiographically confirmed pneumonia, ARDS, and sepsis; they were also more likely to have received antimicrobial agents (Table 4). In addition, patients who were admitted to an ICU or died were older and less likely to have been admitted within 2 days of symptom onset, to have rhinorrhea, to be pregnant, and to have received antivirals within 2 days of symptom onset, as compared with patients who were not admitted to an ICU. In a multivariable logistic model that included age <18 years or ≥18 years, hospital admission ≤2 days or >2 days after the onset of illness, and initiation of antiviral therapy ≤2 days or >2 days after symptom onset, patients who were admitted to the ICU or died were more likely to be adults ≥18 years (odds ratio [OR], 2.0; 95% confidence interval [CI], 1.0–3.9; P=.05) and to have initiated antiviral treatment >2 days after symptom onset (OR, 3.4; 95% CI, 1.3–8.6; P = .01).

Table 4. Clinical characteristics of Patients Hospitalized with 2009 Pandemic Influenza A (H1N1) Virus Infection, comparing Patients not Admitted to the Intensive Care Unit and Survivors versus Hospitalized Intensive Care Unit Patients and Patients who Died, United States, September–October 2009

Clinical characteristic	Hospitalized patients not admitted to the intensive care unit and survivors (n = 166)	Hospitalized patients admitted to the intensive care unit and patient who died (n = 89)
Age, median years (range)[a]	25.5 (1 month to 87 years)	32 (9 months to 70 years)
Age <18 years[a]	65 (39)	21 (24)
Time from illness onset to hospital admission, median days (range)[a,b]	2 (0–27) (n = 166)	3 (0–15) (n = 88)
Length of hospital stay, median days (range)[a,b]	2 (0–22) (n = 164)	8.5 (0–73) (n = 88)
Time from illness onset to discharge or death, median days (range)[a,b]	5 (0–28) (n = 164)	11 (2–82) (n = 88)
Clinical symptoms at hospital admission		
Fever[a]	151 (91)	71 (80)
Cough	144 (87)	75 (84)
Shortness of breath[a]	77 (46)	62 (70)
Wheezing	52 (31)	23 (26)
Fatigue/weakness	57 (34)	35 (39)
Chills	48 (29)	28 (31)
Myalgias	59 (36)	26 (29)
Headache	37 (22)	25 (28)
Altered mental status[a]	11 (7)	14 (16)
Conjunctivitis	2 (1)	3 (3)
Sore throat	43 (26)	24 (27)
Rhinorrhea[a]	73 (44)	22 (25)
Vomiting	58 (35)	24 (27)
Diarrhea[a]	22 (13)	26 (29)
Underlying medical conditions[c]		
Any 1 condition	114 (69)	56 (63)
Asthma or COPD	51 (31)	30 (34)
Diabetes	18 (11)	15 (17)
Chronic cardiovascular disease	19 (11)	16 (18)
Immunocompromised	15 (9)	6 (7)
Chronic renal disease	11 (7)	6 (7)
Neurocognitive disorder	8 (5)	9 (10)
Neuromuscular disorder	10 (6)	9 (10)
Seizure disorder	7 (4)	7 (8)
Pregnancy[a]	24 (14)	5 (6)
Current smoker[c]	26/159 (16)	20/85 (24)
Obese[d]	27/107 (25)	28/78 (36)
Morbidly obese[d]	13/71 (18)	16/61 (26)
Influenza vaccination for seasonal influenza	23/124 (19)	7/50 (14)
Influenza vaccination for pH1N1	4/100 (4)	1/52 (2)

Hospitalization results		
Chest radiograph findings consistent withpneumonia at admission[a]	49/140 (35)	54/85 (64)
Acute respiratory distress syndrome[a]	0/163 (0)	26/76 (34)
Diagnosed with sepsis at hospital admission[a]	2/164 (1)	15/78 (19)
Invasive mechanical ventilation[a]	0/165 (0)	47/79 (59)
Treated with antivirals	132 (80)	76 (85)
Treated with antivirals within 2 days of illness onset[a]	72/131 (55)	25/75 (33)
Treated with antibiotics[a]	105 (63)	81 (91)
Treated with steroids	59 (36)	35 (39)
Among those treated with antivirals, time from illness onset to initiation of antivirals[a], median days (range)	2 (0–27) (n = 131)	4 (0–16) (n = 75)

NOTE. Data are proportion (%) of patients, unless otherwise indicated. Overall missing data for different categories varied. For symptoms, there were 2%–19% of patients with missing data; for underlying conditions, there were 2%–3% with missing data; for influenza vaccination status, there were 32% with missing data; for obesity, there were 5% with missing data; and for hospitalization results, there were 2%–13% with missing data. COPD, chronic obstructive pulmonary disease.

[a] Variables found to be significant ($P<.05$) on bivariate analysis when comparing hospitalized patients (who were not admitted to the intensive care unit and did not die) with patients admitted to the intensive care unit and patients who died. The χ^2 test was used to compare categorical variables, and the Wilcoxon rank-sum test was used to compare continuous variables.

[b] Day of hospital admission was considered hospital day 0.

[c] Patients who are pregnant, immunocompromised (either due to medications or immune disorders including human immunodeficiency syndrome), or have chronic pulmonary (including asthma or COPD), cardiovascular (excludes hypertension), renal, hepatic, hematological, neurological, or metabolic disease (including diabetes) are considered to be at high-risk for influenza-related complications. Patients who are current smokers or obese were not included in groups considered at high-risk for influenza complications.

[d] Body mass index (BMI), calculated as weight in kilograms divided by the square of height in meters, was determined for a subset of patients for whom height and weight data were available to determine obesity (BMI 30–39.9 in adults ⩾18 years or BMI percentile 95–100 in children 2–18 years old) and morbid obesity (BMI ⩾40 in adults only); pregnant women were excluded from this calculation.

DISCUSSION

We report a US case series of patients hospitalized during the fall wave of pH1N1 activity. Our findings were similar to reports from spring 2009 [6–8] and indicate that pH1N1 infection caused severe illness, including pneumonia and ARDS, and resulted in ICU admission of over one-third of patients. Although underlying medical conditions were common, severe illness among young, previously healthy persons also occurred. Antiviral treatment was administered to most patients but was started >2 days after illness onset for the majority of them; this delay in antiviral initiation could contribute to more-severe outcomes, including ICU admission and death. Our data suggest that severity of clinical illness, as measured by the proportion of hospitalized patients admitted to the ICU and the overall hospitalized case fatality proportion, did not change substantially from spring to fall of 2009.

The age distribution of hospitalized patients in both the spring and fall pandemic waves differs from that of hospitalized patients in seasonal influenza epidemics, when influenza hospitalizations are more common among adults ⩾65 years and children <5 years of age [11]. Almost one-half of pH1N1-associated hospitalizations from the fall were of adults in the 18–49-year-old age group, and only 8% were of patients aged ⩾65 years. During the spring pandemic wave, 32%–38% of cases reported occurred among those aged 18–49 years [6–8]. These data support findings in serologic studies that indicate that aging is associated with the presence of cross-reactive immunity and that the prevalence of cross-reactive immunity among children and young adults is rare [17, 18].

Patients in this fall case series presented with fever, cough, shortness of breath, tachypnea, and tachycardia, similar to reports from spring 2009. The acute onset of respiratory illness is typical for influenza [19–22]. In contrast to seasonal influenza, when diarrhea and vomiting have occasionally been reported in children and in <5% of adults [22], vomiting or diarrhea was reported in 41% of patients in this case series. This finding is similar to early reports of pH1N1 infection [7, 8].

Similar to seasonal influenza, patients hospitalized with pH1N1 infection had a high prevalence (67%) of underlying medical conditions. This case series indicates that children hospitalized with pH1N1 infection have a greater frequency of underlying conditions (48%) than do those with seasonal influenza (31%–43%) [10, 23, 24]. In adults, the frequency of underlying conditions in those hospitalized with pH1N1 infection is similar to that for those hospitalized with seasonal influenza [25–27]. Asthma and COPD were the most common underlying conditions in adults in both the spring and fall pandemic waves and are the most common underlying conditions in patients hospitalized with seasonal influenza [10, 23, 25–27]. The frequency of pregnancy (11%) in this case series is similar to that in the spring pandemic wave [7, 8] but is higher than the expected prevalence (1%) in the general population. These data are consistent with seasonal influenza and past

pandemics and indicate that pregnant women are at high risk of severe outcome [28–33]. Data from this case series support Advisory Committee on Immunization Practices (ACIP) recommendations prioritizing pH1N1 vaccination in people with underlying high-risk medical conditions, including pregnant women [16].

In this case series, we obtained data on height and weight or obesity status for almost all patients and found that almost one-half of the patients were obese or morbidly obese. However, >70% of these patients had an underlying condition known to increase their risk for influenza-related complications. For adults in this case series, prevalence of any obesity, defined as BMI ⩾30, was much higher (58%) than the estimated obesity prevalence in the adult US population (34%) [34]. Furthermore, the prevalence of morbid obesity (22%), defined as BMI ⩾40, in this analysis is much higher than the estimated 6% prevalence of morbid obesity in the adult US population [34]. The link between obesity and increased risk of influenza-related complications has been suggested by other studies [6–8, 35] and warrants further investigation.

Few bacterial co-infections were detected, but bacterial diagnostic data were not obtained for all patients, and most received antibiotics near the time of culture collection, potentially reducing diagnostic sensitivity. Thus far during the pH1N1 pandemic, bacterial co-infections have been documented among patients with fatal outcomes from the spring in 46 (28%) of 156 US children with specimens collected from a sterile site or from post-mortem lung biopsy on day of death [36], 8 (38%) of 21 patients with fatal outcome who had undergone autopsy in Brazil [37], and 19 (56%) of 34 patients with fatal outcome who had undergone autopsy in New York City [38]. The most common pathogens identified were *S. aureus* (MRSA and MSSA), *S. pneumoniae*, and *S. pyogenes* [36–38]. In addition to the seasonal and pandemic influenza vaccinations, the 13-valent pneumococcal conjugate vaccine is recommended for all children <5 years of age [39], and the 23-valent pneumococcal polysaccharide vaccine is recommended for all persons aged 2–64 years with certain health conditions and all persons aged ⩾65 years [40].

Although the majority (82%) of patients in this case series were treated with neuraminidase inhibitors, only 47% initiated treatment within 2 days of illness onset. Despite widespread awareness of pH1N1 and antiviral recommendations, initiation of antiviral treatment within 2 days of illness onset did not increase between the spring (45%–51%) and fall [6–8]. Delays in antiviral initiation in both spring and fall waves were correlated with more-severe outcomes of ICU admission and death. Current CDC interim pandemic and seasonal influenza guidelines recommend oseltamivir or zanamivir treatment for hospitalized patients with suspected or confirmed influenza, as well as treatment of outpatients who are at higher risk for complications [41]. Although evidence of antiviral benefit is strongest when treatment is initiated within 2 days of symptom onset, observational data from a prospective cohort study of oseltamivir treatment in elderly hospitalized patients with influenza indicated a reduction in mortality even when antivirals were initiated >2 days after symptom onset [25]. Observational data from Thailand also showed that oseltamivir treatment was associated with survival in hospitalized seasonal influenza patients [42]. The US Food and Drug Administration authorized oseltamivir for treatment of patients with pH1N1 infection after 2 days of illness onset and for treatment of children aged <1 year under an Emergency Use Authorization [41]. Despite the absence of clinical efficacy data, available observational data support recommendations that antiviral therapy should be initiated in hospitalized patients with suspected pH1N1 infection, even if >2 days after illness onset, especially in patients with pneumonia and outpatients who are at higher risk for complications, including pregnant women [41].

Our data are subject to limitations. This case series represents <2% of total hospitalizations with pH1N1 infection reported to the CDC in September and October 2009; however, cases included in the case series were sampled randomly using probability-proportionate-to-size and should be nationally representative. Participation in this case series was voluntary and is therefore subject to reporting bias. In particular, some large states in the Midwest were underrepresented in this case series because of nonparticipation. This case series only includes patients with confirmed pH1N1 infection and may not be representative of hospitalized patients who may have not been tested. Testing and reporting practices could bias these data if only the sickest patients were tested or were reported to health departments. The CDC recommended influenza testing of all hospitalized patients with influenza-like illness [43]; however, all diagnostic testing was performed as clinically indicated, and it is assumed that some patients with influenza were not tested and therefore did not have the opportunity to be included in this case series. Finally, despite use of a standardized data-collection form, not all information was collected for all patients.

Our data suggest that the clinical spectrum of disease and risk factors for severe outcomes do not appear to have changed substantially between the spring and fall pandemic pH1N1 waves. Although influenza activity continues, clinicians should consider influenza, including pH1N1 infection, in the differential diagnosis of patients presenting with fever and respiratory illness or pneumonia. Vaccination with pH1N1 monovalent vaccine should continue according to current ACIP recommendations [44]. Empiric neuraminidase inhibitor treatment for hospitalized patients with suspected influenza or pneumonia or outpatients who have underlying medical

conditions or pregnancy is recommended [41]. The benefits of treatment are greatest when it is started early, but antiviral treatment should not be withheld if patients present >2 days after illness onset.

Acknowledgments

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Financial support. The Influenza Division at the Centers for Disease Control.

Supplement sponsorship. Published as part of a supplement entitled "The 2009 H1N1 Influenza Pandemic: Field and Epidemiologic Investigations," sponsored by the Centers for Disease Control and Prevention.

Potential conflicts of interest. All authors: no conflicts.

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